

L17 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2007:746061 CAPLUS <<LOGINID::20080404>>  
 DOCUMENT NUMBER: 147:101977  
 TITLE: Use of chondroitin sulfate for preparing composition effective for curing human skin diseases  
 INVENTOR(S): Balogh, Tibor; Penyvesi, Geza; Balogh, Gyorgy ; Balogh, Tamas; Hetenyi, Laszlo; Lepenye, Oszkar; Werstros, Janos  
 PATENT ASSIGNEE(S): Hung.  
 SOURCE: Hung. Pat. Appl., Spp.  
 CODEN: HUXXCV  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Hungarian  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 2002003446	A2	20040528	HU 2002-3446	20021014
PRIORITY APPL. INFO.: HU 2002-3446 20021014				

AB The invention concerns chondroitin sulfate-containing ointments for the effective local treatment of dry and/or aging skin and varicose veins. The compound composed of mucopolysaccharide, which is a component of the skin, together with the hyaluronic acid, which has a similar composition, is emptied from the epidermal cells, whose structure changes as a result, it becomes thinner and is not able to bind enough water. Through the addition of chondroitin sulfate, the hyaluronic acid production increases, the adhesion of the horn scales improves, the epidermis becomes thicker and flexible. Furthermore, the composition is effective in the treatment of aesthetically or medically unpleasant skin conditions caused by varicose veins. The chondroitin sulfate is made into a spreadable aqueous composition, together with cosmetol. and pharmaceutically acceptable carriers and fragrances. Thus a cream was prepared from (g): cetyl stearyl alc. 45; stearin 100; glycerin (85%) 100; sorbitol 35; sodium lauryl sulfate 5; chondroitin sulfate sodium salt 5; water 705; 4-hydroxy benzoic acid Me ester 1; ethanol (96%) 10 mL. The cream was stable for at least one year when stored in a closed container at room temperature

L17 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:471969 CAPLUS <<LOGINID::20080404>>  
 DOCUMENT NUMBER: 143:13350  
 TITLE: Pharmaceutical composition comprising a zinc -hyaluronate complex for the treatment of multiple sclerosis  
 INVENTOR(S): Balogh, Gyorgy Tibor; Illes, Janos ; Boros, Andras; Forrai, Gaborne; Szekely, Akosne  
 PATENT ASSIGNEE(S): Richter, Gedeon, Vegyesveti Gyar Rt., Hung.  
 SOURCE: PCT Int. Appl., 21 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049047	A1	20050602	WO 2004-HU107	20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG HU 2003003779 A2 20060228 HU 2003-3779 20031120 EP 1699468 A1 20060913 EP 2004-798745 20041118				

EP 1699468 B1 20070418  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,  
 HR, IS, YU

CN 1882352 A 20061220 CN 2004-80034039 20041118  
 AT 359800 T 20070515 AT 2004-798745 20041118  
 JP 2007512311 T 20070517 JP 2006-540634 20041118  
 ES 2286698 T3 20071201 ES 2004-798745 20041118  
 US 20070123488 A1 20070531 US 2006-579256 20060511  
 IN 2006KN01304 A 20070504 IN 2006-KN1304 20060517  
 NO 2006022857 A 20060818 NO 2006-2857 20060619  
 PRIORITY APPLN. INFO.: HU 2003-3779 A 20031120  
 WO 2004-HU107 W 20041118

AB The invention relates to pharmaceutical compns. for the treatment of  
multiple sclerosis which comprises a zinc-  
hyaluronan complex, preferably a zinc-hyaluronan  
 complex with a mol. weight of 800-1200 kDa, as active ingredient and a  
 pharmaceutically acceptable carrier and/or additive. The process for the  
 preparation of said pharmaceutical compns. as well as the therapeutic use  
 thereof for the treatment of multiple sclerosis are  
 also within the scope of the invention.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2008 ACS ON STN  
 ACCESSION NUMBER: 2005:316333 CAPLUS <<LOGINID::20080404>>  
 DOCUMENT NUMBER: 142360970  
 TITLE: Transdermal pharmaceutical compositions containing  
 polyoxyethylene glyceryl trioleate  
 INVENTOR(S): Eros, Istvan; Pannonhalma Csoka, Ildiko; Soosne  
 Csanyi, Erzsebet; Bodis, Attila; Lapis, Erzsebet;  
 Franciscsne Czinege, Erzsebet; Kissne Csikos, Emonke;  
 Tilles, Janos  
 PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.  
 SOURCE: PCT Int. Appl., 98 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005032514	A1	20050414	WO 2004-HU92	20041006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SI, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 2003003313	A2	20050728	HU 2003-3313	20031009
EP 1673063	A1	20060628	EP 2004-769091	20041006
EP 1673063	B1	20080116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007508287	T	20070405	JP 2006-530614	20041006
AT 383849	T	20080215	AT 2004-769091	20041006
NO 200602053	A	20060508	NO 2006-2053	20060508
US 20070264345	A1	20071115	US 2007-575145	20070323
PRIORITY APPLN. INFO.:			HU 2003-3313	A 20031009
			WO 2004-HU92	W 20041006
AB The invention relates to a liquid crystal gel containing polyoxyethylene glyceryl trioleate, propylene glycol, iso-Pr myristate and a <u>hyaluronic acid salt or complex</u> for use in the manufacture of transdermal pharmaceutical compns. and healing cosmetics. The invention also relates to transdermal pharmaceutical composition consists of an estrogen and a progestin component as well as a liquid crystal gel containing				

polyoxyethylene glyceryl trioleate, propylene glycol, iso-Pr myristate and a hyaluronic acid salt or complex. The invention can be applied for transdermal hormone replacement therapy and for other transdermal depending on the active principles included. Thus, a formulation contained estradiol 0.10, gestodene 0.05 Tagat-TO V 33.30 propylene glycol 16.70, iso-Pr myristate 19.00, EtOH 5.00, benzyl alc. 1.00, sodium hyaluronate 0.10, and water qs to 100 g.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 2003:64403 CAPLUS <LOGINID::20080404>

DOCUMENT NUMBER: 138:265587

TITLE: Effect of different metal ions on the oxidative damage and antioxidant capacity of hyaluronic acid

AUTHOR(S): Balogh, Gyorgy T.; Tilles, Janos;

Szekely, Zsuzsanna; Forrai, Erika; Gere, Aniko

CORPORATE SOURCE: Gedeon Richter Ltd., Budapest, H-1475, Hung.

SOURCE: Archives of Biochemistry and Biophysics (2003),

410(1), 76-82

CODEN: ABBI44; ISSN: 0003-9861

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Degradation and the antioxidant effect of Na<sup>+</sup>, Zn<sup>2+</sup>, Co<sup>2+</sup>, Cu<sup>2+</sup>, and Mn<sup>2+</sup>-hyaluronic acid (HA) assoc. were studied. Our findings revealed the protective effect of certain counterions against ROS-induced HA degradation. We could also sep. the antioxidative effect of certain counterions from that of the HA by examining the effect of the counterions in their free ionic forms. The result showed that metal ions with altering oxidative status (Co<sup>2+</sup>, Cu<sup>2+</sup>, Mn<sup>2+</sup>) proved to be effective in themselves or their effect added to that of HA when HA was also effective. Moreover, the effects of Co-HA against VO<sub>2</sub><sup>-</sup> and of Mn-HA against ONOO<sup>-</sup> as well as the synergic effect of Zn-HA assoc. where Zn<sup>2+</sup> is of fixed oxidative status were attributed to the structure-stabilizing complex formed between certain counterions and HA. Our examination also concerned the influence of HA assoc. on the indirect antioxid. related to Fe<sup>2+</sup> chelating. The individual effects of Zn<sup>2+</sup>, Co<sup>2+</sup>, and Cu<sup>2+</sup> were only detectable, which could be explained by the competitive displacement of ferrous from its binding site.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 2002:748786 CAPLUS <LOGINID::20080404>

DOCUMENT NUMBER: 137:268441

TITLE: Pharmaceutical or cosmetic compositions containing hyaluronic acids

INVENTOR(S): Burger, Kalman; Rethey, Ivan; Stefko, Bela; Gebhardt,

Istvan; Kiraly, Arpadne; Nagy, Geza Takacsi;

Tilles, Janos; Neszmelyi, Erzsébet; Racz,

Istvan; Varkonyi, Victoria

PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt, Hung.

SOURCE: U.S., 17 pp., Cont.-in-part of U. S. 5,472,950.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6458774	B1	20021001	US 1994-345233	19941125
HU 53128	A2	19900928	HU 1989-891	19890224
HU 203372	B	19910729		
WO 9010020	A1	19900907	WO 1990-HU13	19900220
W: AT, AU, BG, CA, CH, DE, DK, ES, FI, GB, JP, KR, LK, LU, NL, NO, RO, SE, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 5554598	A	19960910	US 1992-928154	19920610
US 5472950	A	19951205	US 1992-949030	19920922
PRIORITY APPLN. INFO.:			HU 1989-891	A 19890224

WO 1990-HU13 W 19900220  
 US 1990-602326 B1 19901121  
 US 1992-928154 A2 19920810  
 US 1992-949030 A2 19920922

AB Complexes of deprotonated hyaluronic acid with 3d metal ions of the 4th period of the periodic table and compns. containing these complexes as active ingredients or carriers. A process for the preparation of the complexes and compns. (pharmaceutical and cosmetic compns.) containing these complexes as active ingredients are disclosed in which zinc or cobalt (II) hyaluronate is preferably used as active ingredient. Thus, an injectable solution contained zinc hyaluronate 2.0, and sorbitol 48.3 mg, and water for injection purposes to 1 mL.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2002:685353 CAPLUS <<LOGINID::20080404>>  
 DOCUMENT NUMBER: 138:297239  
 TITLE: Zinc-hyaluronate: an original organotherapeutic compound of Gedeon Richter Ltd  
 AUTHOR(S): Tilles, Janos; Javor, Andras; Szijarto, Elvira  
 CORPORATE SOURCE: Richter Gedeon Rt., Budapest, 1103, Hung.  
 SOURCE: Acta Pharmaceutica Hungarica (2002), 72(1), 15-24  
 CODEN: APHGAO; ISSN: 0001-6659  
 PUBLISHER: Magyar Gyogyszereszeteti Tarsasag  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Hungarian

AB Manufacturing of organotherapeutic products is the most long-standing activity of Gedeon Richter Ltd. dating back to the establishment of the company in 1901. By the 1940s the company had manufactured and marketed about one hundred preps. containing tissue exts. from animals. As a result of the development of synthetic molts., organic therapy fell into the background after World War II. Although the company followed this tendency, it continued manufacturing some organotherapeutic products as well in accordance with the requirements of the time. Since the 1950s the researchers of the company have worked on the research of glycosaminoglycans introducing the manufacture of heparin, and followed by the research of hyaluronic acid (hyaluronan) in the middle of the 1980s. In the human body hyaluronan is one of the main components of the extracellular matrix, where both in passive and active manner it affects the cellular functions through its viscoelastic mol. property and hyaluronan receptors of cells. In certain therapeutic fields such as dermatol., ophthalmol., surgery and rheumatol., these biol. features of hyaluronan are used. Although most of the hyaluronan products contain sodium-hyaluronate (Na-Hy), Richter's researchers found that another metal salt of hyaluronic acid such as zinc-hyaluronate (Zn-Hy) might be more favorable in some therapeutic areas than Na-Hy. Based on this theory, Gedeon Richter Ltd. developed its original zinc associate of hyaluronic acid. It is marketed under the trade name of Curiosin intended for dermatol. application including promoting of wound healing. According to the results of preclin. studies on wound healing the pharmacol. profile of Zn-Hy was more favorable than that of Na-Hy, proving the free radical scavenging, antioxidant, pro inflammatory effects of Zn-Hy as well as the acceleration of chronic wound healing. In clin. studies Curiosin showed its efficacy in the healing of chronic and acute wounds.

L17 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2001:332410 CAPLUS <<LOGINID::20080404>>  
 DOCUMENT NUMBER: 135:92794  
 TITLE: Positron lifetime study of sodium and zinc hyaluronates.  
 AUTHOR(S): Suvegh, K.; Burger, K.; Marek, T.; Vertes, A.; Tilles, J.  
 CORPORATE SOURCE: Eotvos Lorand Tudomanyegyetem, Magkemiai Tanszek, Budapest, 1518, Hung.  
 SOURCE: Acta Pharmaceutica Hungarica (2000), 70(3-6), 77-81  
 CODEN: APHGAO; ISSN: 0001-6659  
 PUBLISHER: Magyar Gyogyszereszeteti Tarsasag  
 DOCUMENT TYPE: Journal

LANGUAGE: Hungarian

AB The aim of this work was to test the positron lifetime technique (PLT) as a tool of the structure study of sodium and zinc hyaluronates. The information based on the PLT measurements (outlined as follows) proved that this method can be useful in this field as well. The lifetime of ortho-positronium (o-Ps) significantly increased and its intensity decreased in the samples containing  $Zn^{2+}$ , compared to Na hyaluronate, indicating that the electronic orbitals are more closed in the case of  $Zn^{2+}$ , and that overlap between the wave functions of the positron and of the electrons decreased. The study of the effect of water content suggested that the hydrogen-bridge-bonds "localized" the free electron pairs. Increasing pressure increased the lifetime and is evidence that the effect of the cations ( $Na^+$  and  $Zn^{2+}$ ) can be explained by change of the electronic structure rather than altering the free vols. of the samples.

L17 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 2001:330863 CAPLUS &lt;&lt;LOGINID:20080404&gt;&gt;

DOCUMENT NUMBER: 135:161590

TITLE: Metal ion coordination of macromolecular bioligands: formation of zinc(II) complex of hyaluronic acid

AUTHOR(S): Burger, K.; Illes, J.; Gyurcsik, B.; Gazdag,

M.; Forral, E.; Dekany, I.; Mihalyfi, K.  
CORPORATE SOURCE: Department of Inorganic and Analytical Chemistry,  
Szeged University, Szeged, H-6701, Hung.

SOURCE: Carbohydrate Research (2001), 332(2), 197-207

CODEN: CRBRAT; ISSN: 0008-6215

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The coordination of Zn(II) ion to hyaluronate (Hya), a natural copolymer, in aqueous solution at pH 6 was studied by potentiometric and CD spectroscopic methods, and by monitoring the changes in macroscopic properties by high-precision measurements. The Zn(II)-selective electrode, and CD measurements proved the binding of Zn(II) by Hya. A number of Hya fragments ( $M_r$  approx.  $3.3 \times 10^3$ - $1.4 \times 10^6$ ) were studied to estimate the contributions of the polyelectrolyte effect, the solvation and host-guest interactions to the extra stabilization of the macromol. Zn(II) complexes as compared with the monomeric unit. The Zn(II) ion activity increase reflected a stability decrease for the fragments with  $M_r < 10^4$ . This mol. weight differs from that where cleavage of the Hya skeleton starts (approx.  $5 \times 10^5$ , according to the size-exclusion gel, and anion-exchange chromatog. behavior of the Hya fragments) and from that where the polyelectrolyte effect stops (approx.  $6 \times 10^3$ ). The excess vols. and Bingham shear yield values of the sols. revealed the transformation of the coherent random coil structure stabilized by intermol. association in the NaHya to an intramol. association producing the globular structure of the ZnHya mol., with a smaller but more strongly bound solvate  $H_2O$  sheet. The binding of Zn(II) by Hya and the rearrangement of the polymer chain, i.e., a size decrease because of the globular structure of the ZnHya mol., as a consequence of the complex formation was proved.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 2000:645863 CAPLUS &lt;&lt;LOGINID:20080404&gt;&gt;

DOCUMENT NUMBER: 133:217693

TITLE: Remedies for joint diseases

INVENTOR(S): Serizawa, Isao; Maekawa, Keisei; Illes, Janos  
; Neszmelli, Erzsebet

PATENT ASSIGNEE(S): Takata Selyaku Co., Ltd., Japan; Richter Gedeon  
Vegyeszeti Gyar Rt.

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.                      KIND      DATE                      APPLICATION NO.                      DATE

WO 2000053194 A1 20000914 WO 2000-JP1487 20000310  
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
JP 2003089647 A 20030328 JP 1999-63718 19990310  
CA 2364451 A1 20000914 CA 2000-2364451 20000310  
EP 1166788 A1 20020102 EP 2000-908017 20000310  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, SE, MC, PT, SI, SL, LT, LV, FI, RO  
EE 200100478 A 20030217 EE 2001-478 20000310  
EE 4660 B1 20060815  
JP 3751202 B2 20060301 JP 2000-603683 20000310  
US 6608043 B1 20030819 US 2001-936245 20010907  
BG 105885 A 20020628 BG 2001-105885 20010910  
JP 1999-63718 A 19990310  
WO 2000-JP1487 W 20000310

## PRIORITY APPLN. INFO.:

AB Remedies for joint diseases such as rheumatoid arthritis contain as the active ingredient a complex (associate) of hyaluronic acid with zinc. Compared with hyaluronic acid and zinc (i.e., constituents thereof), this complex synergistically inhibits the proliferation of synovial cells and thus regulates the production of a histoclastic enzyme MMP-9 produced by synovial cells.  
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1998:719278 CAPLUS <<LOGINID::20080404>>  
DOCUMENT NUMBER: 129:347309  
TITLE: Use of zinc hyaluronate against peptic ulcer  
INVENTOR(S): Szporny, Laszlo; Matuz, Judit; Neszmelyi, Erzsebet; Forrai, Gaborne; Zsoka, Erika; Stefok, Bela; Saghy, Katalin  
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.; Szporny, Gyula; Illes, Janos  
SOURCE: PCT Int. Appl., 55 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848815	A1	19981105	WO 1998-HU44	19980428
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
HU 9700826	A1	19981228	HU 1997-826	19970429
HU 225991	B1	20080228		
CA 2286756	A1	19981105	CA 1998-2286756	19980428
CA 2286756	C	20080219		
AU 9873468	A	19981124	AU 1998-73468	19980428
AU 749757	B2	20020704		
EE 9900470	A	20000615	EE 1999-470	19980428
EE 4953	B1	20080215		
BR 9809354	A	20000704	BR 1998-9354	19980428
EP 1017403	A1	20000712	EP 1998-920684	19980428
EP 1017403	B1	20060322		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, SE, PT, IE, SI, SL, LT, LV, FI, RO, CY				

NZ 500978	A	20010525	NZ 1998-500978	19980428
JP 2001522361	T	20011113	JP 1998-546388	19980428
TW 501927	B	20020911	TW 1998-87106525	19980428
CN 1126548	B	20031105	CN 1998-804672	19980428
PL 189526	B1	20050831	PL 1998-336482	19980428
SK 284864	B6	20060105	SK 1999-1468	19980428
AT 320814	T	20060415	AT 1998-920684	19980428
PT 1017403	T	20060731	PT 1998-920684	19980428
ES 2259813	T3	20061016	ES 1998-920684	19980428
CZ 297317	B6	20061115	CZ 1999-3827	19980428
ZA 9803626	A	19981105	ZA 1998-3626	19980429
RG 64458	B1	20050331	RG 1998-103822	19990119
NO 9905229	A	19991222	NO 1999-5229	19991026
MX 9909943	A	20000430	MX 1999-9943	19991028
HK 1025250	A1	20040611	HK 2000-104494	20000720
US 6656921	B1	20031202	US 2000-403714	20000921

## PRIORITY APPLN. INFO.:

HU 1997-826	A	19970429
WO 1998-H044	W	19980428

AB The invention relates to pharmaceutical compns. against peptic ulcer as well as a process for the preparation. The pharmaceutical compns. of the comprise zinc associate (complex) of hyaluronic acid as an active ingredient in admixt. with a carrier and/or other additives commonly used in the pharmaceutical industry. Thus, tablets (200 mg) contained zinc hyaluronate 10, anhydrous lactose 106, pregelatinized starch (Lycatos PGS) 6, corn starch 40, microcryst. cellulose (Avicel PH 102) 30, Aerosil-200 1, talc 6, and magnesium stearate 1 mg. Zinc hyaluronate inhibited gastric lesions at 25, 50, and 100 mg/kg p.o.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 1998:365862 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 129:113401

TITLE: Filtration of solutions with high viscosity; from the laboratory experiments to the production

AUTHOR(S): Bodis, Attila; Benkoczy, Zoltan; Gondar, Erzsebet;

Tilles, Janos; Neszmelyi, Erzsebet

CORPORATE SOURCE: Richter Gedeon Vegyeszeti Gyar Rt., Budapest, H-1475, Hung.

SOURCE: Acta Pharmaceutica Hungarica (1998), 68(2), 127-132

CODEN: APHGAQ; ISSN: 0001-6659

PUBLISHER: Magyar Gyogyszereszeti Tarassag

DOCUMENT TYPE: Journal

LANGUAGE: Hungarian

AB Zinc hyaluronate is useful for wound healing. The task was the elaboration of the sterile filtration technol. of the 0.2% solution. In the first step, 0.2  $\mu$ m pore diameter filters were used. During scale-up, filter boards are not suitable. The filtration time increased and sometimes the whole process stopped because of the relatively small filtration area. For larger batches, polypropylene capsule filters have been applied. The mean pore diameter of the filter was 0.2  $\mu$ m, but because of the irregular pore size distribution, the filtrate was not sterile. In the next experience, the inlet pore diameter was 0.65  $\mu$ m, and the outlet pore diameter 0.45  $\mu$ m. This filtration process resulted in a sterile filtrate with reduced active content. This means that the solution has been ultrafiltered. Applying high pressure forms a compact layer on the filter's surface, which is functioning as a secondary filter layer. The filtration should begin with low pressure and it has to increase gradually from 0 to 2 bar, in 0.5 bar steps. Depending on the concentration, above 35-45% the active content of the filtrate decreased. The filtration of these products is very difficult even at laboratory scale.

L17 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 1998:180769 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 128:248593

TITLE: Pharmaceutical compositions with antimicrobial activity

INVENTOR(S): Tilles, Janos; Neszmelyi, Erzsebet; Stefko,

Bodis, Burget, Kalman

PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.

SOURCE: PCT Int. Appl., 31 pp.

DOCUMENT TYPE: CODEN: PIXXD2  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: English  
 PATENT INFORMATION: 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810773	A1	19980319	WO 1997-HU52	19970911
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MX, MY, NZ, PE, PG, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW RW: CH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BE, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
HU 9602498	A2	19980428	HU 1996-2498	19960912
HU 9602498	A3	19980528		
HU 225329	B1	20060928		
AU 9744691	A	19980402	AU 1997-44691	19970911
CN 1230117	A	19990929	CN 1997-197886	19970911
CN 1130204	B	20031210		
EP 964687	A1	19991222	EP 1997-943084	19970911
EP 964687	B1	20031126		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001900860	T	20010123	JP 1998-513414	19970911
RU 2204394	C2	20030520	RU 1999-107569	19970911
AT 254922	T	20031215	AT 1997-943084	19970911
PT 964687	T	20040227	PT 1997-943084	19970911
ES 2212131	T3	20040716	ES 1997-943084	19970911
US 6348190	B1	20020219	US 1999-254386	19990304
HU 1996-2498 A 19960912 WO 1997-HU52 W 19970911				
AB The invention relates to pharmaceutical compns. of antimicrobial effect as well as a process for the preparation thereof. The pharmaceutical compns. of the invention comprise <u>zinc</u> or cobalt <u>hyaluronate</u> associate (complex) as active ingredient in admixt. with a carrier and/or other additives commonly used in the pharmaceutical industry. Antimicrobial activities of 0.2 % <u>Zn hyaluronate</u> were studied against various microbes in vitro. A topical gel containing 0.2 % <u>Zn hyaluronate</u> was also formulated.				
REFERENCE COUNT:	4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT			

L17 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1996:34869 CAPLUS <LOGINID:20080404>  
 DOCUMENT NUMBER: 124:97766  
 TITLE: Cobalt and zinc hyaluronic acid complexes for treatment of wounds and ulcers  
 INVENTOR(S): Burger, Kalman; Rethely, Ivan; Stefkó, Bela; Gebhardt, Istvan; Kiraly, Arpadné; Nagy, Geza T.; Tiles, Janos; Neszmelyi, Erzsebet; Racz, Istvan; Varkonyi, Viktoria  
 PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.  
 SOURCE: U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 928,154. CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5472950	A	19951205	US 1992-949030	19920922
HU 53128	A2	19900928	HU 1989-891	19890224
HU 203372	B	19910729		
US 5554598	A	19960910	US 1992-928154	19920810
US 6458774	B1	20021001	US 1994-345233	19941125
HU 1989-891 A 19890224 US 1990-602326 B2 19901121 US 1992-928154 A2 19920810				
PRIORITY APPLN. INFO.:				



WO 1990-HU13 W 19900220  
US 1992-949030 A2 19920922

AB Stoichiometric complexes of deprotonated hyaluronate acid with 3d metal ions of the 4th period of the Periodic Table are useful as active ingredients in compns. for healing and reepithelialization of crural and decubitus ulcers, nonhealing wounds, burns, and acne. In the  $Zn^{2+}$  and  $Co^{2+}$  complexes, each metal atom is surrounded by 4 O atoms in the 1st coordination sphere, with  $Zn-O$  and  $Co-O$  bond lengths of 199 and 197 pm, resp., as shown by EXAFS studies.  $Na^+$  is bound by hyaluronate acid to a lesser degree. Zn hyaluronate was more effective than  $Na^+$  hyaluronate in promoting healing of crural ulcers. A topical aqueous solution was formulated containing Zn hyaluronate 5.0, K sorbate 1.0, and NaOAc 24.6 mg/mL.

L17 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1993:220701 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 118:220701

TITLE: Hyaluronate-metal ion interactions: correlations between viscometric, potentiometric, polarographic and electrophoretic data

AUTHOR(S): Sipos, P.; Veber, Margit; Burger, K.; Tilles, J.; Machula, G.

CORPORATE SOURCE: Dep. Inorg. Anal. Chem., A. Jozsef Univ., Szeged, H-6701, Hung.

SOURCE: Acta Chimica Hungarica (1992), 129(5), 671-83  
CODEN: ACHUDG; ISSN: 0231-3146

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The interactions between sodium hyaluronate and different mono- and bivalent cations ( $H^+$ ,  $K^+$ ,  $Ag^+$ ,  $Cu^{2+}$ ,  $Ca^{2+}$ ,  $Cd^{2+}$ , and  $Pb^{2+}$ ) were studied via potentiometry using ion-selective electrodes, polarog., viscometry and paper-electrophoretic measurements. The electrochem. methods led to conditional stability consts. useful for characterizing the strengths of interactions and for determining the preference sequence of the metal ions studied. The decrease in dynamic viscosity ( $\eta$ ) following the addition of metal ions to hyaluronate solution reflects the same sequence of strengths of interaction. In the presence of  $Cu^{2+}$  ions, flow-shear hysteresis was found, the magnitude of which was closely connected with the equilibrium-chemical properties of the  $Cu^{2+}$  hyaluronate system.

L17 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1992:608168 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 117:208168

TITLE: Utilization of enzymic digestion for the study of the macromolecular effect in complexation processes. Protonation and copper coordination equilibria of hyaluronate and its fragments

AUTHOR(S): Burger, Kalman; Sipos, Pal; Tilles, Janos

CORPORATE SOURCE: Dep. Inorg. Anal. Chem., A. Jozsef Univ., Szeged, Hung.

SOURCE: Bulletin of the Chemical Society of Japan (1992), 65(8), 2211-14

CODEN: BCSJAB; ISSN: 0009-2673

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of enzymic digestion on the proton and copper(II) binding ability of hyaluronate (HYA), a macromol. polyelectrolyte, and its fragments were studied via potentiometry. The degree of depolymn. was measured by spectrophotometry. The log  $K_{app}$  vs.  $\alpha$  functions (where  $\alpha$  is the mole fraction of dissociated carboxyl groups in the samples) and the protonation group consts. were determined in the native and enzymically partly and completely decomposed samples. The two different data treatments led to the same chemical consequences. The interaction between copper(II) and HYA was less dependent on the degree of depolymn. than that between  $H^+$  and HYA, the results indicating an almost negligible role of long-range electrostatic forces in the copper(II)-HYA interaction. All the investigations demonstrated that enzymic digestion can be used advantageously for the characterization of the macromol. effect in coordination processes.

L17 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1991:129118 CAPLUS &lt;&lt;LOGINID:20080404&gt;&gt;

DOCUMENT NUMBER: 114:129118

TITLE: Hyaluronic acid metal complexes for epithelization acceleration

INVENTOR(S): Takacs Nagy, Geza; Takacs, Nagy Geza; Rethey, Ivan; Tilles, Janos; Stefkó, Bela; Neszemlyi, Erzsebet; Gebhardt, Istvan; Racz, Istvan; Kiraly, Arpad, Mrs.; Varkonyi, Viktoria

PATENT ASSIGNEE(S): Richter, Gedeon, Vegyeszeti Gyar Rt., Hung.

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXX02

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9010020	A1	19900907	WO 1990-HU13	19900220
W: AT, AU, BG, CA, CH, DE, DK, ES, FI, GB, JP, KR, LK, LU, NL, NO, RO, SE, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
HU 53128	A2	19900928	HU 1989-891	19890224
HU 203372	B	19910729		
CA 2027596	A1	19900825	CA 1990-2027596	19900220
CA 2027596	C	20010102		
AU 9051088	A	19900926	AU 1990-51088	19900220
AU 623232	B2	19920507		
EP 413016	A1	19910220	EP 1990-903397	19900220
EP 413016	B1	19931222		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 03505231	T	19911114	JP 1990-503644	19900220
JP 2571312	B2	19970116		
AT 98964	T	19940115	AT 1990-903397	19900220
ES 2061016	T3	19941201	ES 1990-903397	19900220
ZA 9001357	A	19901128	ZA 1990-1357	19900222
DD 292263	A5	19910725	DD 1990-338061	19900222
IL 93489	A	19940530	IL 1990-93489	19900222
CZ 281050	B6	19960515	CZ 1990-857	19900222
SK 279830	B6	19981202	SK 1990-857	19900222
CN 1045394	A	19900919	CN 1990-100904	19900223
CN 1024557	B	19940518		
CN 1086422	A	19940511	CN 1993-109689	19900223
CN 1051228	B	20000412		
FI 101707	B	19980814	FI 1990-5109	19901017
FI 101707	B1	19980814		
NO 9004584	A	19901221	NO 1990-4584	19901023
NO 301169	B1	19970922		
RU 2099350	C1	19971220	RU 1990-4831382	19901023
RU 2021304	C1	19941015	RU 1991-4895005	19910411
LV 10112	B	19950220	LV 1992-687	19921230
LV 10965	B	19960820	LV 1993-747	19930629
LT 3806	B	19960325	LT 1993-1418	19931026
LT 3873	B	19960425	LT 1993-1474	19931118
US 6458794	B1	20021001	US 1994-345233	19941125
PRIORITY APPL. INFO.:			HU 1989-891	A 19890224
			EP 1990-903397	A 19900220
			WO 1990-HU13	A 19900220
			US 1990-602326	B1 19901121
			US 1992-928154	A2 19920810
			US 1992-949030	A2 19920922

AB Complexes of deprotonated hyaluronic acid with Co or Zn are prepared as active ingredients in cosmetics or drugs for the treatment of crural ulcer, decubitus ulcer, wounds, burns, etc. Topical application of a solution of 0.2% Zn hyaluronate in isotonic sorbitol to patients with crural ulcer led to acceleration of epithelization. Zn hyaluronate was prepared by the reaction of ZnCl<sub>2</sub> with Na hyaluronate, in aqueous medium.

L17 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1970:9791 CAPLUS &lt;&lt;LOGINID:20080404&gt;&gt;

DOCUMENT NUMBER: 72:9791  
 ORIGINAL REFERENCE NO.: 72:1763a,1766a  
 TITLE: Iron-alum method for elective demonstration of acid mucopolysaccharides. II  
 AUTHOR(S): Torok, Laszlo J.; Kovacs, Laszlo; Balogh, Gyorgy  
 CORPORATE SOURCE: Med. Univ. Budapest, Budapest, Hung.  
 SOURCE: Acta Biologica Academiae Scientiarum Hungaricae (1969), 20(3), 319-24  
 CODEN: ABAHAU; ISSN: 0001-5288  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Pretreatment of cartilage with iron-alum demonstrated that structures containing acid mucopolysaccharides (I) stained selectively with certain basic dyes. This staining was due to 2 factors: first to the blocking action of Fe ions which form stable bonds with phosphate and carboxyl ions and 2nd to the looser linkage between Fe ions and sulfate groups, which, according to the principle of competitive antagonism, enables I to bind the mols. of basic dyes. The polyanions of I did not react with basic dyes when blocked by methylation or treatment with cetylpyridinium bromide; the reactions were also neg. when the procedure was followed by Fe-alum treatment. After hyaluronidase digestion, the cartilaginous substance failed to bind basic dyes, while its Fe-binding capacity, although less pronounced, remained demonstrable; previous trypsin digestion did not weaken the staining reaction of I, but it did weaken that of the surrounding tissues, whereas papain digestion diminished the intensity of staining. Furthermore, the protein component of chondroprotein and mucoprotein, when in a stable form, is able to bind Fe ions; this phenomenon is probably involved in the mechanism through which dye is bound by intact chondromucoprotein.